Remarks

Reconsideration of the above identified application is respectfully requested.

Claims 1-21 remain on the application. The new claims find support in the specification and particularly in the Examples.

Before responding to the specific objections of the examiner, the invention will be described in detail. The present invention relates to a method of reducing the amount of β-1,6 linked chains in cell wall glucans from yeast, resulting in an improved product with respect to immunomodulatory abilities. The crucial step is to remove the β-1,6-linked chains without altering the β-1,6-linked branching points from which also β-1,3-linked side chains extend from, i.e. leaving the "original" structure of the yeast cell wall glucan. This can be done chemically by acid degradation, but using acid also might jeopardize the essential β-1,3-linked side chains (that as stated above is anchored to the main chain through a β-1,6-linkage), or it is insufficient needing repeated extractions with a weak acid. In the present application this is overcome by using an endo-β-1,6-glucanase that specifically cleaved off the unwanted β-1,6-glucan chains leaving a much more potent product, indifferent of purification degree, as compared to the starting material. It is, of course, not novel that an endo-β-1,6-glucanase cleaves off β-1,6-linked chains also in yeast, as β-1,6-linkages are known to be present in yeast, however, the novelty in the present inventors relates to the use of the enzyme to remove the β-1,6-linked chains. In the present invention, a skilled worker in the art is able to prepare a more immunologically active product than

the starting material. This could not be anticipated by any of the references cited in the Office Action. In the presently claimed invention a β-glucan (whether it is soluble or the insoluble), is prepared that has maintained it's branched structure, but where essentially all β-1,6-linked chains have been removed, which chains reduce the immunological activity of the glucan. Subsequently, what remains, and is claimed in the present invention, is a product having the highly branched nature, but where the side chains are showing β-1,3-linkages (except for the single anchoring point linking the side chain to the main chain an anchoring point that has to be a β-1,6-linkage).

Claims 20-21 been rejected under 35 USC § 112, first paragraph, as failing to comply with a written description requirement. The examiner believes that the new language in Claim 20 requiring "four or less β-1,6-bound glucose units" lacks support in this specification as filed. This phrase appears in many of the claims.

The examiner states on page 5 of the Office Action that "Rather, page 4, line 9-16, of this specification describes the molecule wherein either most or essentially all of the short β-1,6 linked branches of four glucose units or fewer have been removed". This is a mischaracterization of the text, for on the contrary, the specification states: "The β-1,6 glucanase enzyme cleavage insures that most chains of more than four β-1,6 bound glucans units are cleaved off". The reason for the limit of four, is that the endo-enzyme preferentially would cleave pentamers and larger, but would leave chains of up to tetramers near their branching point, or other linkages. Therefore, the reasoning supports the language claimed in the application, i.e., "being essentially free of β-1,6 linked chains or having a maximum chain with a link of four glucose units." Applicants respectfully request the examiner to reconsider the position.

Concerning the examiners interpretation of word "most" Applicants respectfully disagree. Applicants do not believe that the term "most" as

described as "more than 50 percent" is definite. Applicants believe that interpretation of the word "most" is closer to "almost all" and to "more than half". Further, it is respectfully submitted one skilled in art recognize the explanation concerning the number of glucose units and therefore, recognize the phrase "essentially free" as being compatible with the interpretation found in specification and claims. Therefore, Applicants believe this term has sufficient definiteness for the one skilled in the art to notice the invention.

Claims 1, 4, 5, 7, 9, 10, 13, 14, and 16, 19 have been rejected under 35 USC § 102, as being anticipated by the Shiota et al. reference. The β-1,6-glucanase used by the Shiota et al reference is different from the microorgranism that is used and claimed by Applicants. The microorganisms used by Applicants are included in the claim language of the application. Further, the claimed invention relates to a glucan comprised of β-1,3-linked glucose units and is essentially free of β-1,6-linked chains apart from those chains of four or less β-1,6-bound glucose units. In addition, the Shiota reference does not include any description of immunostimulatory or immunomodulatory ability of the resulting glucan products. The Shiota et al. reference describes the method of characterising β-glucanse from yeast and nothing else. The presently claimed invention describes an entirely diverse invention.

Claims 1, 2, 4, 5, 7, 9, 10, 13, 14, and 16-19 have been rejected under 35 USC § 102, (b) as being anticipated by the Yamamoto et al. reference. The Yamamoto et al. reference discloses a glucanase derived from a different microorganism than those described and claimed in the present invention. The Yamamoto reference cannot anticipate the presently claimed invention because of this reason. Applicants respectfully request that the rejection be withdrawn.

Claims 20 and 21 have been rejected 35 USC § 102 (e) being anticipated by Rorstad at all reference. The presently claimed invention is an improvement

over the product of Rorstad et al. reference. The presently claimed invention shows that by reducing the amount of β-1,6 linked chains, without altering the remaining branches, provides an improved product with biological activities greater than that of the starting material, and therefore greater than the products made by the process of Rorstad et al. reference. Clearly, the Rorstad et al reference does not anticipate the improved claimed invention of the present application.

Claims 1-3 have been rejected under 35 USC § 103 (a) as being unpatentable over the Shiota et al. or the Yamamoto et al. reference, a view of the de la Cruz reference. The examiner states that Claims 2 and 3 limit the β-1,6 glucanse to an enzyme obtained from *Trichoderma harzianum*. The combination of references does not lead one skilled in the art to the presently claimed invention. The Shiota at all reference does not disclose the immunostimulatory nor the immunomodulatory ability of the resulting glucans, as claimed in the present invention. Nor does it describe the microorganisms responsible for the glucanse used in the presently claimed invention. The Yamamoto and de la Cruz references when added to the teachings of the Shioda et al reference still do not suggest the presently claimed invention. The use of the different microorganisms to produce glucocanase does not render obvious the presently claimed invention, because the immunosimulatory nor the immunomodulatory effects of the product are the disclosed. Clearly, the references taken singly or in combination do not suggest the presently claim invention.

Claims 1,6, and 13-15 have been rejected under USC § 103(a) as being unpatentable over the Shiota et al reference in view of Jamas reference, U. S Patent No. 5,028,703. The Shiota et al reference does not disclose processes that suggest the process recited in Claims 6 and 16 are. Indeed, there is no reference or disclosure in the Jamas reference teaching the removal of β-1,6 linked chains should result in a product with improved immunomodulatory

activity. Thus, this fact alone distinguishes the claimed invention from the Jamas reference. The Jamas reference can be combined with the Shiota reference or any other pior art reference and still, this fact remains.

Claims 10 and 11 have been rejected under USC 35 § 103 (a) as being unpatentable over the Shiota et al reference in view of the Jamas reference and further, in view of the Matsueda et al reference. The reasoning recited above applies to the rejection alleged in these references. The use of formic acid as a pre-enzymatic hydrolyzing agent disclosed by the Matsueda reference does not distinguish the combination of teachings to have them render obvious the claimed invention. The Jamas reference does not disclose immunostimulatory or immunomodulatory abilities of the glucan as does the claimed invention. Therefore, this combination of references like the other combinations suggested by the examiner, do not suggest the presently claimed invention.

In view for foregoing, Applicants submit that the claims meet the requirements of 35 United States Code. Therefore, an early notice of allowance of the above identified application is respectfully requested.

Respectfully submitted,

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